Genome-wide Regulation of 5hmC, 5mC, and Gene Expression by Tet1 Hydroxylase in Mouse Embryonic Stem Cells.

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Public Summary:
DNA methylation at the 5 position of cytosine (5mC) in the mammalian genome is a key epigenetic event critical for various cellular processes. The ten-eleven translocation (Tet) family of 5mC-hydroxylases, which convert 5mC to 5-hydroxymethylcytosine (5hmC), offers a way for dynamic regulation of DNA methylation. Here we report that Tet1 binds to unmodified C or 5mC- or 5hmC-modified CpG-rich DNA through its CXXC domain. Genome-wide mapping of Tet1 and 5hmC reveals mechanisms by which Tet1 controls 5hmC and 5mC levels in mouse embryonic stem cells (mESCs). We also uncover a comprehensive gene network influenced by Tet1. Collectively, our data suggest that Tet1 controls DNA methylation both by binding to CpG-rich regions to prevent unwanted DNA methyltransferase activity, and by converting 5mC to 5hmC through hydroxylase activity. This Tet1-mediated antagonism of CpG methylation imparts differential maintenance of DNA methylation status at Tet1 targets, ultimately contributing to mESC differentiation and the onset of embryonic development.

Scientific Abstract:
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